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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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WARNER-LAMBERT COMPANY
2800 PLYMOUTH RD
ANN ARBOR, MI 48105

EXAMINER	
HENLEY III, RAYMOND J	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 04/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/724,856	FRAIL ET AL.	
	Examiner	Art Unit	
	Raymond J. Henley III	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-25 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-25 is/are rejected.

7)☒ Claim(s) 11 and 22 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 6/1/2004.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

CLAIMS 1-25 ARE PRESENTED FOR EXAMINATION

Applicants' Information Disclosure Statement filed June 1, 2004 has been received and entered into the application. As reflected by the attached, completed copy of form PTO-1449, the Examiner has considered the cited references.

Claim Objection

Claims 11 and 22 are objected to because of the following informality. Appropriate correction is required.

In claim 11, line 1, "pynmidinyl" should read ---pyrimidinyl--- and at line 3, "puninyl" apparently should read ---purinyl---.

In claim 22, lines 1-2, "comprising a mixture...the S or R configuration" should be rewritten as follows in order to clearly indicate that the subject matter of claim 1 is further limited: ---of claim 1, wherein the compound of formula (1) is a mixture of stereoisomers wherein the carbon atom designated * is in the R or S configuration---.

Claim Rejection - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the treatment or management (see the specification at page 20, line 33 for support) of migraine headaches, does not reasonably provide enablement for the prevention of the same. The specification does not enable any person skilled in the art to which

it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Burden on the Examiner for Making a Rejection Under 35 U.S.C. § 112 First Paragraph for Lack of Enablement

As set forth in *In re Marzocchi*, 169 USPQ 367, 370 (CCPA 1971):

"[A] [s]pecification disclosure which contains teaching of manner and process of making and using the invention in terms corresponding to the scope to those used in describing and defining subject matter sought to be patented must be taken as in compliance with enabling requirement of first paragraph of 35 U.S.C. 112 *unless there is reason to doubt the objective truth of statements contain therein which must be relied on for enabling support*; assuming that sufficient reason for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis, such a rejection can be overcome by suitable proofs indicating that teaching contained in specification is truly enabling." (emphasis added).

Here, the objective truth of the statement that migraine headaches can be prevented is doubted because the term "prevent" is synonymous with the term "curing" and both circumscribe methods of absolute success. Because absolute success is not reasonably possible with most diseases/disorders known to one skilled in the art, the specification, which lacks an objective showing that migraine headaches can actually be prevented, is viewed as lacking an enabling disclosure of the same. It is noted that the term "prevent" does not *necessarily* mean that something is kept from ever occurring, but it *is* an interpretation that falls under the "broad and reasonable" standard for claim term interpretation as set forth in the MPEP at § 2111 and thus is proper.

Further supporting the Examiner's doubt that migraine headaches may actually be prevented is the Couch et al. reference cited by Applicants (reference "AI"). In particular, the authors report that the known "prophylactic" anti-migraine agents, methysergide and

amitriptyline, were only effective in providing a percentage of relief in a percentage of patients tested (see page 121, the abstract and col. 1, second paragraph). Thus, even the art recognized prophylactic agents were unable to keep migraine headaches from occurring and this casts doubt on whether Applicants' compound could actually do what has not been done before, i.e., actually keep migraine headaches from occurring.

Thus, because of the above reasons, the Examiner doubts the objective truth of the statement that the presently claimed compounds could prevent migraine headaches and the Examiner has therefore satisfied the burden as set forth in *In re Marzocchi, Id.* for making a rejection under 35 U.S.C. § 112, first paragraph. The claims are therefore deemed properly rejected.

In order to overcome the present rejection, Applicants may wish to consider either deleting the term "preventing" from claim 1, line 1 or replacing it with "managing". As noted above, support for the concept of managing migraine headaches is found in the present specification at page 20, line 33.

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beck et al. (WO 01/32625, cited by Applicants, reference "AE") in view of Couch et al. (cited by Applicants, reference "AI").

Beck et al. teach a method for treating "analgesia" which comprises administering a therapeutically effective amount of the claimed tetrahydroisoquinoline compounds to a subject in need thereof (see the abstract, page 4, line 1 – page 18, line 31, page 21, line 12 and page 32, line 27).

The difference between the above and the claimed subject matter lies in that Beck et al. fail to expressly disclose a method for the treatment of chronic or neuropathic pain or of treating migraine headache.

However, the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because the term "analgesia" in Beck et al. would have been reasonably interpreted as pain by one of ordinary skill in the art. This would be the case because "analgesia" means the lack of pain, and thus it would not have been reasonable to take the disclosure of Beck et al. to mean that the compounds would be effective for the treatment of *a lack of* pain. Given, therefore, that the reference discloses, in an unlimited manner, the treatment of pain, one of ordinary skill in the art

would have been motivated to employ the compounds of Beck et al. for the treatment of pain in general and thus would have recognized that pain of various etiologies, including pain lasting over a period of time, i.e., chronic, pain of a neurological origin, i.e., neuropathic, or pain from headaches, such as a migraine (see Couch et al. at page 122, col. 1, penultimate paragraph "unilateral pain, bilateral pain, throbbing pain, steady pain and neck pain") could have been treated with a reasonable expectation that such pain could be successfully relieved.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Provisional

Claims 1-25 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3 and 9 of copending Application No. 10/426,097, in view of Couch et al. (reference "AI", cited by Applicants).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the differences between the currently claimed subject matter and that of the co-pending claims are:

(i) the current application includes claims of intermediate, i.e., present claims 2-19, and narrow, i.e., present claim 23, scope as compared to the claims of the co-pending application which are more narrow than the independent claims of the co-pending application; and

(ii) co-pending claim 9 recites "analgesia" as disorder to be treated while the present claims are directed to the treatment chronic or neuropathic pain or migraine headache.

However, to the skilled artisan, the subject matter of the co-pending and present claims would have been obvious, when view each in light of the other, because:

(i) as can be readily determined by a comparison of the variable groups in both sets of claims, the tetrahydroisoquinoline compounds of the present claims are included in the metes and bounds of the co-pending claims and the selection of any particular compound, or group of compounds, from those disclosed in the co-pending claims would have been a matter well within the purview of the skilled artisan; and

(ii) the term "analgesia" in co-pending claim 9 would have been reasonably interpreted as pain by one of ordinary skill in the art. This would be the case because "analgesia" means the lack of pain, and thus it would not have been reasonable to take the disclosure of the co-pending claim to mean that the compounds would be effective for the treatment of *a lack of* pain. Given, therefore, that the co-pending claim includes, in an unlimited manner, the treatment of pain, one of ordinary skill in the art would have been motivated to employ the compounds of the co-pending claims for the treatment of pain in general and thus would have recognized that pain of various etiologies, including pain lasting over a period of time, i.e., chronic, pain of a neurological origin, i.e., neuropathic, or pain from headaches, such as a migraine (see Couch et al. at page 122, col. 1, penultimate paragraph "unilateral pain, bilateral pain, throbbing pain,

steady pain and neck pain") could have been treated with a reasonable expectation that such pain could be successfully relieved.

The statement that the "analgesia" is a condition "created by or is dependent upon decreased availability of serotonin, norepinephrine or dopamine" (co-pending claim 3) is not seen to distinguish the current claims over the co-pending claims because in both sets of claims, the painful conditions apparently would have been the same.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The reference cited by the Examiner on the attached form PTO-892 and not relied on is included to show the general state of the art.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond J. Henley III whose telephone number is 571-272-0575. The examiner can normally be reached on M-F, 8:30 am to 4:00 pm Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Raymond J Henley III
Primary Examiner
Art Unit 1614

April 12, 2005